COOPERATION TREATY

by fax and post

From the INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

J.A. KEMP & Co
REC'D - 2 OCT 2000
Action by.....

PCT

To:

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NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	25.09.00
Applicant's or agent's file reference: N.78459DMG/TJD	IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US99/09346	30/04/1999	01/05/1998

Applicant: CHIRON CORPORATION et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Büchler, S Tel. +49 89 2399-8090

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
N.78459DMG/TJD		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US99/09346	30/04/1999	01/05/1998
International Patent Classification (IPC) or national classification and IPC		
C12N15/31		
Applicant		
CHIRON CORPORATION et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☒ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the International application
   - VIII ☒ Certain observations on the International application

Date of submission of the demand	Date of completion of this report
01/12/1999	25.09.00
Name and mailing address of the international preliminary examining authority:	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Rojo Romeo, E Telephone No. +49 89 2399 7321

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US99/09346

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-1419	as originally filed				

Claims, pages:

1-18	as received on	04/09/2000	with letter of	04/09/2000	

Drawings, sheets:

1/31-31/31	as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

II. Priority

1. ☒ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

   ☒ copy of the earlier application whose priority has been claimed.

   ☐ translation of the earlier application whose priority has been claimed.

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US99/09346

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1, 3, 16, 18 (entirely); 2, 4-15, 17 (partially).

because:

☒ the said international application, or the said claims Nos. 1, 3, 6, 18 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1, 3, 16, 18 (entirely); 2, 4-15, 17 (partially).

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:

see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☐ all parts.

☒ the parts relating to claims Nos. 2, 4-15, 17 (partially).

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 2, 4-15, 17 (partially)
	No:	Claims
Inventive step (IS)	Yes:	Claims 2, 4-15, 17 (partially)
	No:	Claims
Industrial applicability (IA)	Yes:	Claims 2, 4-15, 17 (partially)
	No:	Claims

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

Th following defects in the form or contents of the international application have been noted:

see separate sheet

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US99/09346

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

INTERNATIONAL PRELIMINARY EXAMINATION REPORT - SEPARATE SHEET

International application No. PCT/US99/09346

Re Item II

Priority

The right of priority was not assessed because the priority document is missing.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The applicant failed to pay additional examination fees and requested in his letter of 21.07.00 that this International Preliminary Examination Report be established on the basis of Invention 5 (SEQ ID No: 1201/1202).

Consequently, claims 2, 4-15 and 17 are examined as far as these claims concern SEQ ID No. 1201/1202.

Claims 1, 3, 16 and 18 are disregarded.

Re Item IV

Lack of unity of invention

The objection for lack of unity raised by the International Search authority is maintained by the International Examination Authority. The International Search Authority found this application to contain 1510 different inventions. Search fees were paid for 8 inventions. Thus, the current application concerns 8 different inventions:

invention 1 (claims 1, 3, 16, 18, all completely; 2, 4-15, 17, all partially)

A protein comprising the amino acid sequence of SEQ ID NO: 2790 or comprising a fragment of at least 7 (preferably consecutive) amino acids of said SEQ ID NO; a protein having 50% or greater homology to said protein(s); an antibody binding to said protein(s); a nucleic acid encoding said protein(s), preferably comprising the nucleotide sequence of SEQ ID NO: 2789 or a fragment comprising 10 or more consecutive nucleotides thereof; complementary nucleic acid molecules; compositions comprising said protein(s), nucleic acid(s) or antibody for vaccination, diagnosis or pharmaceutical use, preferably immunogenic compositions comprising said protein(s), and the use of said composition(s).

invention 2 (claims 2, 4-15, 17, all partially)

A protein comprising the amino acid sequence of SEQ ID NO: 2 or comprising a fragment of at least 7 consecutive amino acids of said SEQ ID NO; an antibody binding to said protein(s); a nucleic acid encoding said protein(s), preferably comprising the nucleotide

sequence of SEQ ID NO: 1 or a fragment comprising 10 or more consecutive nucleotides thereof; complementary nucleic acid molecules; compositions comprising said protein(s), nucleic acid(s) or antibody for vaccination, diagnosis or pharmaceutical use, preferably immunogenic compositions comprising said protein(s), and the use of said composition(s).

invention 3 (claims 2, 4-15, 17, all partially)
As invention 2 but concerning SEQ ID NO: 441/442, respectively.

invention 4 (claims 2, 4-15, 17, all partially)
As invention 2 but concerning SEQ ID NO: 489/490, respectively.

invention 5 (claims 2, 4-15, 17, all partially)
As invention 2 but concerning SEQ ID NO: 1201/1202, respectively.

invention 6 (claims 2, 4-15, 17, all partially)
As invention 2 but concerning SEQ ID NO: 1455/1456, respectively.

invention 7 (claims 2, 4-15, 17, all partially)
As invention 2 but concerning SEQ ID NO: 1745/1746, respectively.

invention 8 (claims 2, 4-15, 17, all partially)
As invention 2 but concerning SEQ ID NO: 2791/2792, respectively.

Only invention 5 (SEQ ID No.: 1201/1202) is examined (see Item III).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: ROKBI B ET AL.: 'Evaluation of recombinant transferrin - binding protein B variants from Neisseria meningitidis for their ability to induce cross-reactive and bactericidal antibodies against a genetically diverse collection of serogroup B strains.' INFECTION AND IMMUNITY, vol. 65, no. 1, January 1997 (1997-01), pages 55-63, XP002138643

D2: DATABASE GCG_GENESEQ [Online] ID W14640, AC W14640, 5 March 1998

(1998-03-05) QUENTIN-MILLET M J ET AL.: 'N. meningitidis HTR Tbp2 (del3777-385, del407-465, del488-508)' XP002138654 -& WO 97 13860 A (PASTEUR MERIEUX SERUMS VACC; QUENTIN MILLET MARIE JOSE (FR); ROKBI)) 17 April 1997 (1997-04-17)

Document D1 discloses recombinant transferrin binding proteins (Tbp) from Neisseria meningitidis capable of inducing cross-reactive and bactericidal antibodies against various serogroup B neisseria species.
Document D2 discloses the sequence of a Tbp protein having 23,5% identity to SEQ ID No.: 1202 of the present application.

None of the documents cited in the International Search Report discoses the claimed subject-matter. The current set of claims is thus considered novel over these documents.

Inventive step (Art. 33(3) PCT)
Document D2 can be considered as the closest prior art since it concerns a protein from Neisseria meningitidis useful as immunogenic component of broad spectrum vaccines. The problem underlying the current application is the provision of alternative sequences of proteins useful as antigens for the generation of antibodies. The solution provided by the present application is the provision of nucleic acid and protein of SEQ ID No.: 1201/1202. However, none of the documents cited in the International Search Report would have allowed the skilled person to achieve said subject-matter (full length sequence) in an obvious manner. Therefore, inventive step can be acknowledged for this novel Neisseria meningitidis antigen.

Re Item VII

Certain defects in the international application

The following back reference was read as bellow:
in claim 7 to claim 6 instead of claim 5

Re Item VIII

Certain observations on the international application

1. Clarity (Art. 6 PCT)
   Claim 17 is read as being directed to a composition per se comprising the product of claim 2, and thus, being equivalent to claim 12 as far as the latter concerns the

protein of claim 2.

2. Support by specification (Art. 6 PCT) in combination with Art. 5 PCT (complete and enabling disclosure)
There are no experiments which provide evidence that the specific protein, antibodies or nucleic acid could be successfully used as a medicament or pharmaceutical. All evidence provided was in vitro (e.g. Fig 8). Therefore, claims 13-15 are not supported by the specification.

AK+34

CLAIMS

1. A protein comprising a fragment of an amino acid sequence from SEQ ID NO: 2790 wherein said fragment comprises at least 7 amino acids from said sequence.

2. A protein comprising an amino acid sequence selected from the group consisting of even numbered SEQ IDs from SEQ ID NO: 2 through to SEQ ID NO: 3020.

3. A protein having 50% or greater homology to a protein according to claim 1.

4 A protein comprising a fragment of an amino acid sequence selected from the group consisting of even numbered SEQ IDs from SEQ ID NO: 2 through SEQ ID NO: 3020, wherein said fragment comprises 14 or more consecutive amino acids from said sequence.

5. An antibody which binds specifically to a protein according to any one of claims 1 to 3.

6. A nucleic acid molecule which encodes a protein according to any one of claims 1 to 3.

7. A nucleic acid molecule according to claim 5, comprising a nucleotide sequence selected from the group consisting of odd numbered SEQ IDs from SEQ ID NO: 1 through to SEQ ID NO: 3019.

8. A nucleic acid molecule comprising a fragment of a nucleotide sequence selected from the group consisting of odd numbered SEQ IDs from SEQ ID NO: 1 through SEQ ID NO: 3019, wherein said fragment comprises 40 or more consecutive nucleotides from said sequence.

9. A nucleic acid molecule comprising a nucleotide sequence complementary to a nucleic acid molecule according to claim 6.

10. A nucleic acid molecule comprising a nucleotide sequence complementary to a nucleic acid molecule according to claim 7.

11. A nucleic acid molecule comprising a nucleotide sequence

complementary to a nucleic acid molecule according to claim 8.

12. A composition comprising a protein, a nucleic acid molecule, or an antibody according to any preceding claim.

13. A composition according to claim 12 being a vaccine composition or a diagnostic composition.

14. A composition according to claim 12 for use as a pharmaceutical.

15. The use of a composition according to claim 12 in the manufacture of a medicament for the treatment or prevention of infection due to Neisserial bacteria.

16. A composition comprising a protein of claim 1 wherein said composition is immunogenic.

17. A composition comprising a protein of claim 2 wherein said composition is immunogenic.

18. A composition comprising a protein of claim 3 wherein said composition is immunogenic.